39. EMERGING INFECTIONS AND BIOTERRORISM

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INTRODUCTION

There have been events in the recent past that demonstrate that terrorist attacks on civilians are a real threat. These attacks have not always been successful, but they demonstrate that the threat is real: The World Trade Center bombing, New York, N.Y. (1993) Federal building bombing, Oklahoma City, Okla., Centennial Olympic Park bombing, Atlanta, Ga., Sarin release, Tokyo, Japan, Anthrax hoaxes, Washington, D.C., Las Vegas, Nev., and other locations, and the Embassy bombings, Kenya and Tanzania.

There are three important factors in the decision to use or not to use a biological weapon: motives, capabilities and financial resources.

BIOTERRORISM THREAT AGENTS

What are the agents that can be considered for use in a terrorist attack? There are eight "classic" biological warfare agents that can be considered the classic or core bioterrorist agents: these are the organisms or toxins that cause the diseases anthrax, botulism, brucellosis, plague, Q fever, smallpox, staphylococcal enterotoxins and tularaemia. Three other disease-causing agents that could be used are cholera, salmonellosis, and shigellosis. In addition to these diseases and agents, there are the "emerging infections", leptospirosis, chlamydial pneumonia, Lyme disease, Legionnaire's pneumonia, Ehrilichiosis, glanders, Vancomycin resistant enterococci and Escherichia coli strain O157:H7. Table 1 lists the new or emerging viruses and the diseases they cause. Some of the illnesses or symptoms that may result from using these bioterrorist agents are:

- Encephalitis
- Hemorrhagic mediastinitis
- Pneumonia with abnormal liver function tests
- Papulopustular rash
- Hemorrhagic fever
- Descending paralysis
- Nausea, vomiting, diarrhea
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In addition to these, there is concern about the viral hemorrhagic fevers caused by a variety of viruses. These are listed in Table 2. Although these viruses come from different families or genuses, they have several properties in common and some differences as well. These are:

- Small RNA viruses
- Lipid enveloped and acid sensitive
- Aerosol infectivity
- Persist in nature, but different strategies
- Negative, positive, ambisense replication strategies
- Different morphology and morphogenesis
- Interactions with cells differ: cytopathic effects, interferon sensitivity
- Disease syndrome similar, pathogenesis differs
- Human immune response differs

EFFECTIVENESS OF BIOTERRORISM AGENTS

How effective can these bioterrorism agents be? Most scenarios involve releasing these agents in the air because the respiratory exposure route is the best way to reach the largest number of people quickly.

Effects of dissemination of 50 kg of a biological agent downwind from an airplane toward a city of 500.000 people:

Agent or disease	**km**	**Dead**	**Iincapacitated**
Venezuelan equine encephalitis	1	400	35,000
Tick-borne encephalitis virus	1	9,500	35,000
Q fever	>20	150	125,000
Tularemia	>20	30,000	125,000
Anthrax spores	>20	95,000	125,000

In order to release the agents in the air, the stability of the aerosol becomes important. The stability of aerosols is given by the amount of degradation in percent that occurs over time, often expressed as percent/minute. The smaller the number, the more stable the aerosol. Aerosol stabilities of some viruses are given below:

Virus	**percent degraded/min**
Vaccinia virus	0.3
Influenza virus	1.9
Venezuelan equine encephalitis	3.0
Marburg virus (saliva)	11.5
Marburg virus (+10% glycerin)	1.5

NATURAL OUTBREAK VS. BIOTERRORISM

Emerging disease agent could be used as bioterrorist weapons because little will be known about the disease as it emerges. Therefore naturally emerging infectious disease outbreaks could be mistaken for bioterrorism. Some examples of unusual outbreaks that could have been mistaken for bioterrorism are given below:

Event/Disease	**Location**	**Year**
Legionnaires' disease outbreak	Philadelphia	1976
Rift Valley fever	Egypt	1977
Urban Q fever	Nova Scotia	1987
Botulism	Egypt	1991
Vibrio Cholerae O 139	Bangladesh, India	1992
Hantavirus pulmonary syndrome	United States	1993
Plague	India	1994
Food-borne cryptosporidiosis	Minnesota	1995
Ebola virus infection	Zaire	1995
Antibiotic-resistant strain of Plague	Madagascar	1995
Monkypox	Zaire	1996
Antibiotic-resistant Anthrax	India	1997
Nipah virus encephalitis	Malaysia, Singapore	1998-1999

It may be difficult to differentiate between natural outbreaks emerging diseases and outbreaks of these same diseases that are caused by intentional releases of agents. Here is a list of some the characteristics of outbreak, which suggest the possibility of intentional use of

an emerging infectious agent. Especially in the case of newly emerging diseases, this type of assessment may not be able to be made until after the characteristics of the diseases and disease-causing agent are examined and understood.

- Outbreak of a rare disease
- Outbreak of a disease in an area where it is not normally endemic
- Occurrence of a seasonal disease during the wrong time of the year
- Attribution of an outbreak caused by a known pathogen to a strain with an unusual antimicrobial pattern.
- Unusual age distribution of persons involved in an outbreak
- Other unusual epidemiological features of an outbreak due to a known pathogen
- Unusual clinical presentation associated with a known pathogen

BIOLOGICAL AGENT PREPARATION

There are some common features to preparing a biological agent to be used in bioterrorism. First the initial bacterial or virus strain must be obtained. Then it must be cultured to a high titer in sufficient quantities to be effective when released. The cultured agent must be processed to permit dissemination as an aerosol or other form if desired. The cultured, processed agent must be stable enough for storage in the processed form. This processed form should be tested for effectiveness and dissemination. And then finally, it must be disseminated for effect.

FIGURES AND TABLES

Table 1. New and reemerging viruses

Viruses	**Date**	**Genus**
New		
Human herpesvirus 6 (HHV-6)	1986	herpesvirus
Human herpesvirus 7 (HHV-7)	1990	herpesvirus
GS viruses (hepatitis)	1994	Flavivirus
Human herpesvirus 8 (HHV-8)	1995	herpesvirus
Reemerging		
Cocoa swollen shoot		Badnavirus
Dengue		Bunyavirus
Ebola		Flavivirus
Equine morbillivirus	1994	Morbillivirus
Hantaan group		Bunyaviruses
Phocine distemper	1987	Morbillivirus
Rabbit calicivirus disease /Viral hemorrhagic disease	1985	Calicivirus
Rift Valley fever		Bunyaviruses
Tomato spotted wilt		Bunyavirus
Whitefly-transmitted Geminiviruses (group III Geminiviruses)		Geminivirus

Table 2. Viral Hemorrhagic Fevers

Family and/or genus	**Disease(s)**
Arenaviridae	Lassa fever, Bolivian HF (Machupo virus), Argentine HF (Junin virus), other South American HF
Bunyaviridae	
Phlebovirus	RVF
Nairovirus	Crimean-Congo HF
Hantavirus	HF with renal syndrome, hantavirus Syndrome
Filovirus	Marburg HF, Ebola HF
Flavivirus	Yellow fever, dengue HF, tick-borne flavivirus HF

KEY WORDS:
Emerging infections, biological and toxin agents, bioterrorism